

What is claimed is:

1. A model of an Fc receptor (FcR) protein, wherein said model represents a three dimensional structure that substantially conforms to the atomic coordinates of Table 1.

2. The model of Claim 1, wherein said structure substantially conforms to the atomic coordinates and B-values represented by Table 1.

3. The model of Claim 1, wherein said structure is monomeric.

4. The model of Claim 1, wherein said structure is dimeric.

5. The model of Claim 1, wherein said structure substantially conforms to the atomic coordinates of a table selected from the group consisting of Table 2, Table 3, Table 4 and Table 5.

6. The model of Claim 1, wherein at least about 50% of said structure has an average root-mean-square deviation (RMSD) of less than about 1.5Å for backbone atoms in secondary structure elements in each domain of said structure.

7. The model of Claim 1, wherein at least about 50% of common amino acid side chains between said structure and a structure comprising said atomic coordinates have an average root-mean-square deviation (RMSD) of less than about 1.5Å.

8. The model of Claim 1, wherein said FcR protein comprises an amino acid sequence that is at least about 25% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:12.

9. The model of Claim 1, wherein said FcR protein comprises an amino acid sequence that is at least about 40% identical to an amino acid sequence selected from the group

consisting of SEQ ID NO:3, SEQ ID NO:10, SEQ ID NO:11 and SEQ
ID NO:12.

10. The model of Claim 1, wherein said FcR protein comprises an amino acid sequence that is at least about 60% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:10, SEQ ID NO:11 and SEQ
ID NO:12.

11. The model of Claim 1, wherein said FcR protein comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, a mutant of any of said amino acid sequences, and an allelic variant of any of said amino acid sequences.

12. The model of Claim 1, wherein said FcR protein comprises an amino acid sequence selected from the group consisting of: an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13; a mutant of SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 or SEQ ID NO:13; and an allelic variant of SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 or SEQ ID NO:13.

13. The model of Claim 1, wherein said FcR protein is selected from the group consisting of FcγRI protein, FcγRIIa protein, FcγRIIb protein, FcγRIIc protein, FcγRIII protein, FcεRI protein, FcαRI protein and structural homologues of any of said FcR proteins.

14. The model of Claim 1, wherein said FcR protein is selected from the group consisting of FcγRI protein, FcγRIIa

protein, FcγRIIb protein, FcγRIIc protein, FcγRIII protein, FcεRI protein and FcαRI protein.

15. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcγRIIa protein monomer, an FcγRIIa protein dimer and structural homologues of said FcγRIIa proteins.

16. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcεRI protein dimer, an FcεRI protein monomer and structural homologues of said FcεRI proteins.

17. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcγRI protein dimer, an FcγRI protein monomer and structural homologues of said FcγRI protein.

18. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcγRIIb protein dimer, an FcγRIIb protein monomer and structural homologues of said FcγRIIb protein.

19. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcγRIIc protein dimer, an FcγRIIc protein monomer and structural homologues of said FcγRIIc protein.

20. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcγRIIIb protein dimer, an FcγRIIIb protein monomer and structural homologues of said FcγRIIIb protein.

21. The model of Claim 1, wherein said FcR protein is selected from the group consisting of an FcαRI protein dimer, an FcαRI protein monomer and structural homologues of said FcαRI protein.

22. The model of Claim 1, wherein said atomic coordinates are generated by the method comprising:

(a) providing an FcγRIIa protein in crystalline form;

5 (b) generating an electron-density map of said crystalline FcγRIIa protein; and

(c) analyzing said electron-density map to produce said atomic coordinates.

23. The model of Claim 22, wherein said crystalline FcγRIIa protein is produced by a method comprising: combining FcγRIIa protein with a mother liquor buffer selected from the group consisting of an acetate salt buffer and a sulphate buffer, and inducing crystal formation to produce said
5 crystalline FcγRIIa protein.

24. The model of Claim 23, wherein said acetate buffer comprises about 200 mM ammonium acetate, about 100 mM sodium citrate and about 30% PEG 4000, said buffer having a pH of about 5.6.

25. The model of Claim 23, wherein said sulphate buffer comprises about 0.1 M HEPES and about 1.5 M lithium sulphate, said buffer having a pH of about 7.5.

26. The model of Claim 22, wherein said step of generating an electron-density map comprises analyzing said crystalline FcγRIIa protein by X-ray diffraction.

27. The model of Claim 22, wherein said crystalline FcγRIIa protein is derivatized in Di-γ-iodo bis{ethylenediamine} di Platinum(II) nitrate prior to said X-ray diffraction.

28. The model of Claim 22, wherein said crystalline FcγRIIa protein is derivatized in about 5 mM Di-γ-iodo bis[ethylenediamine] di Platinum(II) nitrate prior to said X-ray diffraction.

29. The model of Claim 1, wherein said model is a computer image generated by a computer-readable medium encoded

with a set of three dimensional coordinates of said three dimensional structure, wherein, using a graphical display software program, said three dimensional coordinates create an
5 electronic file that can be visualized on a computer capable of representing said electronic file as a three dimensional image.

30. A computer-assisted method of structure based drug design of bioactive compounds, comprising:

a. providing a model of an Fc receptor (FcR) protein, wherein said model represents a three dimensional structure that substantially conforms to the atomic coordinates of Table 1;

b. designing a chemical compound using said model; and,

c. chemically synthesizing said chemical compound.

31. The method of Claim 30, wherein said method further comprises:

d. evaluating the bioactivity of said synthesized chemical compound.

32. The method of Claim 30, wherein said three dimensional structure comprises the atomic coordinates listed in Table 1.

33. The method of Claim 30, wherein said three dimensional structure is dimeric.

34. The method of Claim 30, wherein said three dimensional structure comprises the atomic coordinates listed in a table selected from the group consisting of Table 2, Table 3, Table 4, and Table 5.

35. The method of Claim 30, wherein said model comprises a computer image generated when the atomic coordinates listed in Table 1 are analyzed on a computer using a graphical display software program to create an electronic file of said image and visualizing said electronic file on a computer capable of representing said electronic file as a three dimensional image.

36. The method of Claim 30, wherein said step of designing comprises computational screening of one or more databases of chemical compounds in which the three dimensional structure of said compounds are known.

37. The method of Claim 36, further comprising interacting a compound identified by said screening step with said model by computer.

38. The method of Claim 30, wherein said step of designing comprises directed drug design.

39. The method of Claim 30, wherein said step of designing comprises random drug design.

40. The method of Claim 30, wherein said step of designing comprises grid-based drug design.

41. The method of Claim 30, wherein said step of designing comprises selecting compounds which are predicted to mimic said three dimensional structure of said FcR protein.

42. The method of Claim 30, wherein said step of designing comprises selecting compounds which are predicted to bind to said three dimensional structure of said FcR protein.

43. The method of Claim 30, wherein said bioactivity is selected from the group consisting of inhibiting binding of said FcR protein to an immunoglobulin protein, binding to said FcR protein, binding to an immunoglobulin which is capable of binding to said FcR protein, inhibiting phagocytosis of said immunoglobulin protein, inhibiting dimerization of said FcR protein, stimulating cellular signal transduction through said FcR protein, and stimulating release of cytokines through said FcR protein.

44. The method of Claim 30, wherein said FcR protein is FcγRIIIa and said bioactivity is selected from the group consisting of inhibiting binding of FcγRIIIa protein to IgG, inhibiting phagocytosis of IgG, inhibiting dimerization of FcγRIIIa protein, stimulating cellular signal transduction through an FcγRIIIa protein, stimulating release of cytokines selected from the group consisting of IL-6 and IL-12.

45. The method of Claim 30, wherein said FcR protein is FcγRIIIb and said bioactivity is selected from the group consisting of inhibiting binding of FcγRIIIb protein to IgG, inhibiting phagocytosis of IgG, inhibiting dimerization of FcγRIIIb protein, stimulating cellular signal transduction through an FcγRIIIb protein, stimulating release of cytokines selected from the group consisting of IL-6 and IL-12.

46. The method of Claim 30, wherein said FcR protein is FcεRI and said bioactivity is selected from the group consisting of inhibiting binding of FcεRI protein to IgE, inhibiting phagocytosis of IgE, inhibiting dimerization of FcεRI protein, stimulating cellular signal transduction through an FcεRI protein, stimulating release of histamine and serotonin by mast cells and inhibiting release of histamine and serotonin by mast cells.

47. A computer-assisted method of structure based drug design of bioactive compounds, comprising:

a. providing a model of an Fc receptor (FcR) protein, wherein said model represents a three dimensional structure that substantially conforms to the atomic coordinates selected from the group consisting of atomic coordinates represented by Table 1; atomic coordinates represented by Table 2; atomic coordinates represented by Table 3; atomic coordinates represented by Table 4; and atomic coordinates represented by Table 5;

- b. designing a chemical compound using said model; and,
c. chemically synthesizing said chemical compound.

48. A computer-assisted method of structure based drug design of bioactive compounds, comprising:

- a. providing a model of a three dimensional structure of an Fc receptor (FcR) protein selected from the group consisting of FcγRIIa, FcγRIIb and FcεRI;
- b. designing a chemical compound using said model; and,
- c. chemically synthesizing said chemical compound.

49. A three dimensional computer image of the three dimensional structure of an FcR protein.

50. The image of Claim 49, wherein said structure substantially conforms with the three dimensional coordinates selected from the group consisting of the three dimensional coordinates listed in Table 1; the three dimensional coordinates listed in Table 2; the three dimensional coordinates listed in Table 3; the three dimensional coordinates listed in Table 4; and the three dimensional coordinates listed in Table 5.

51. The image of Claim 49, wherein said computer image is generated when a set of three dimensional coordinates comprising said three dimensional coordinates are analyzed on a computer using a graphical display software program to create an electronic file of said image and visualizing said electronic file on a computer capable of representing electronic file as a three dimensional image.

52. The image of Claim 49, wherein said three dimensional computer image is represented by a two dimensional image selected from the group consisting of Fig. 4, Fig. 6, Fig. 7, Fig. 8, Fig. 9, Fig. 10, Fig. 14, Fig. 15 and Fig. 16.

53. The image of Claim 49, wherein said three dimensional computer image is used to design a therapeutic compound.

54. A computer-readable medium encoded with a set of three dimensional coordinates of an FcR protein having a three dimensional structure that substantially conforms to the atomic coordinates of Table 1, wherein, using a graphical display software program, said three dimensional coordinates create an electronic file that can be visualized on a computer capable of representing said electronic file as a three dimensional image.

55. A computer-readable medium encoded with a set of three dimensional coordinates selected from the group consisting of the three dimensional coordinates represented in Table 1, the three dimensional coordinates represented in Table 2, the three dimensional coordinates represented in Table 3, the three dimensional coordinates represented in Table 4, and the three dimensional coordinates represented in Table 5, wherein, using a graphical display software program, said three dimensional coordinates create an electronic file that can be visualized on a computer capable of representing said electronic file as a three dimensional image.

56. A model of the three dimensional structure of an FcR protein selected from the group consisting of FcγRI protein, FcγRIIb protein, FcγRIIc protein, FcγRIIIb protein, FcεRI protein and FcαRI protein, said model being produced by the method comprising:

- (a) providing an amino acid sequence of an FcγRIIa protein and an amino acid sequence of said FcR protein;
- (b) identifying structurally conserved regions shared between said FcγRIIa amino acid sequence and said FcR protein amino acid sequence; and
- (c) determining atomic coordinates for said FcR protein by assigning said structurally conserved regions of said FcR protein to a three dimensional structure using a three dimensional structure of said FcγRIIa protein which substantially conforms to the atomic coordinates represented in Table 1, to derive a model of said three dimensional structure of said FcR protein amino acid sequence.

57. The model of Claim 56, wherein said FcγRI protein amino acid sequence comprises SEQ ID NO:7; wherein said FcγRIIb protein amino acid sequence comprises SEQ ID NO:5; wherein said FcγRIIc protein amino acid sequence comprises SEQ ID NO:6; wherein said FcγRIIIb protein amino acid sequence comprises SEQ ID NO:8; wherein said FcεRI protein amino acid sequence comprises SEQ ID NO:9; and wherein said FcαRI protein amino acid sequence comprises SEQ ID NO:13.

58. A therapeutic composition that, when administered to an animal, reduces IgG-mediated tissue damage, said therapeutic composition comprising an inhibitory compound that inhibits the activity of an Fcγ receptor (FcγR) protein, said inhibitory compound being identified by the method comprising:

(a) providing a three dimensional structure of an FcγR protein selected from the group consisting of FcγRI, FcγRIIa, FcγRIIb, FcγRIIc and FcγRIIIb, wherein said three dimensional structure of said FcγR protein substantially conforms to atomic coordinates represented by Table 1;

(b) using said three dimensional structure of said FcγR protein to design a chemical compound selected from the group consisting of a compound that inhibits binding of FcγR protein to IgG, a compound that substantially mimics the three dimensional structure of FcγR protein and a compound that inhibits binding of FcγR protein with a molecule that stimulates cellular signal transduction through an FcγR protein;

(c) chemically synthesizing said chemical compound; and

(d) evaluating the ability of said synthesized chemical compound to reduce IgG-mediated tissue damage.

59. The composition of Claim 58, wherein said IgG-mediated tissue damage results from a biological response selected from the group consisting of IgG-mediated hypersensitivity, IgG-mediated recruitment of inflammatory cells, and IgG-mediated release of inflammatory modulators.

60. The composition of Claim 58, wherein said structure substantially conforms with the atomic coordinates represented in Table 1.

61. The composition of Claim 58, wherein said chemical compound is selected from the group consisting of an inorganic compound and an organic compound.

62. The composition of Claim 58, wherein said chemical compound is selected from the group consisting of oligonucleotides, peptides, peptidomimetic compounds and small organic molecules.

63. The composition of Claim 58, wherein said chemical compound is selected from the group consisting of an analog of said FcγR protein, a substrate analog of said FcγR protein and a peptidomimetic compound of said FcγR protein.

64. The composition of Claim 58, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant, and a carrier.

65. A therapeutic composition that, when administered to an animal, enhances IgG-mediated responses, said therapeutic composition comprising a stimulatory compound that stimulates the activity of an Fcγ receptor (FcγR) protein, said
5 stimulatory compound being identified by the method comprising:

(a) providing a three dimensional structure of an FcγR protein selected from the group consisting of FcγRI, FcγRIIa, FcγRIIb, FcγRIIc and FcγRIIIb, wherein said three
10 dimensional structure of said FcγR protein substantially conforms to atomic coordinates represented by Table 1;

(b) using said three dimensional structure of said FcγR protein to design a chemical compound selected from the group consisting of a compound that stimulates binding of FcγR
15 protein to IgG, a compound that substantially mimics the three dimensional structure of FcγR protein and a compound that stimulates binding of FcγR protein with a molecule that stimulates cellular signal transduction through an FcγR protein;

(c) chemically synthesizing said chemical compound;
20 and

(d) evaluating the ability of said synthesized chemical compound to enhance IgG-mediated responses.

66. A therapeutic composition that, when administered to an animal, reduces IgE-mediated responses, said therapeutic composition comprising an inhibitory compound that inhibits the activity of an Fcε receptor I (FcεRI) protein, said inhibitory compound being identified by the method comprising:

(a) providing a three dimensional structure of an FcεRI protein, wherein said three dimensional structure of said FcεRI protein substantially conforms to the atomic coordinates selected from the group consisting of the atomic coordinates represented by Table 1, the atomic coordinates represented by Table 2, the atomic coordinates represented by Table 3, the atomic coordinates represented by Table 4 and the atomic coordinates represented by Table 5;

(b) using said three dimensional structure of said FcεRI protein to design a chemical compound selected from the group consisting of a compound that inhibits binding of FcεRI protein to IgE, a compound that substantially mimics the three dimensional structure of FcεRI protein and a compound that inhibits binding of FcεRI protein with a molecule that stimulates cellular signal transduction through an FcεRI protein;

(c) chemically synthesizing said chemical compound; and

(d) evaluating the ability of said synthesized chemical compound to reduce IgE-mediated responses.

67. The composition of Claim 66, wherein said IgE-mediated response results from a biological response selected from the group consisting of IgE-mediated hypersensitivity, IgE-mediated recruitment of inflammatory cells, and IgE-mediated release of inflammatory modulators.

68. The composition of Claim 66, wherein said structure comprises the atomic coordinates represented in Table 3.

69. The composition of Claim 66, wherein said structure comprises the atomic coordinates represented in Table 4.

70. The composition of Claim 66, wherein said chemical compound is selected from the group consisting of an inorganic compound and an organic compound.

71. The composition of Claim 66, wherein said chemical compound is selected from the group consisting of oligonucleotides, peptides, peptidomimetic compounds and small organic molecules.

72. The composition of Claim 66, wherein said chemical compound is selected from the group consisting of an analog of said FcεR protein, a substrate analog of said FcεRI protein and a peptidomimetic compound of said FcεRI protein.

73. The composition of Claim 66, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant, and a carrier.

74. A therapeutic composition that, when administered to an animal, enhances IgE-mediated responses, said therapeutic composition comprising a stimulatory compound that stimulates the activity of an Fcε receptor I (FcεRI) protein, said
5 stimulatory compound being identified by the method comprising:

(a) providing a three dimensional structure of an FcεRI protein, wherein said three dimensional structure of said FcεRI protein substantially conforms to the atomic
10 coordinates selected from the group consisting of the atomic coordinates represented by Table 1, the atomic coordinates represented by Table 2, the atomic coordinates represented by Table 3, the atomic coordinates represented by Table 4 and the atomic coordinates represented by Table 5;

(b) using said three dimensional structure of said FcεRI protein to design a chemical compound selected from the group consisting of a compound that stimulates binding of FcεRI protein to IgE, a compound that substantially mimics the three dimensional structure of FcεRI protein and a compound
15 that stimulates binding of FcεRI protein with a molecule that stimulates cellular signal transduction through an FcεRI protein;

(c) chemically synthesizing said chemical compound;
and

(d) evaluating the ability of said synthesized
25 chemical compound to enhance IgE-mediated responses.

75. A method to determine a three dimensional structure of an FcR protein, said method comprising

(a) providing an amino acid sequence of an FcR protein selected from the group consisting of FcγRI protein, FcγRIIb protein, FcγRIIc protein, FcγRIIIb protein, FcεRI protein and FcαRI protein, wherein the three dimensional structure of said FcR protein is not known;

(b) analyzing the pattern of folding of said amino acid sequence in a three dimensional conformation by fold recognition; and

(c) comparing said pattern of folding of said FcR protein amino acid sequence with the three dimensional structure of FcγRIIa protein to determine the three dimensional structure of said FcR protein, wherein said three dimensional structure of said FcγRIIa protein substantially conforms to the atomic coordinates represented in Table 1.

76. A method to derive a model of the three dimensional structure of an FcR protein, said method comprising the steps of:

5 (a) providing an amino acid sequence of an FcγRIIa protein and an amino acid sequence of an FcR protein;

(b) identifying structurally conserved regions shared between said FcγRIIa amino acid sequence and said FcR protein amino acid sequence;

10 (c) determining atomic coordinates for said target structure by assigning said structurally conserved regions of said FcR protein to a three dimensional structure using a three dimensional structure of an FcγRIIa protein based on atomic coordinates that substantially conform to the atomic coordinates represented in Table 1 to derive a model of the
15 three dimensional structure of said FcR protein amino acid sequence.

77. The method of Claim 76, further comprising assigning atomic coordinates for side chains of said FcR protein by determining sterically allowable positions using a library of rotamers.

78. A method to derive a three dimensional structure of a crystallized FcR protein, said method comprising the steps of:

5 (a) comparing the Patterson function of a crystallized FcR protein with the Patterson function of crystalline FcγRIIa protein to produce an electron-density map of said crystallized FcR protein; and

10 (b) analyzing said electron-density map to produce said three dimensional structure of said crystallized FcR protein.

79. The method of Claim 78, further comprising the step of electronically simulating said three dimensional structure of said crystallized FcR protein to derive a computer image of said three dimensional structure of said crystallized FcR protein.

5 80. The method of Claim 78, further comprising the step of rotating said Patterson function of said crystallized FcR protein on said Patterson function of said crystalline FcγRIIa protein to determine the correct orientation of said crystallized FcR protein in a crystal of said crystallized FcR protein to identify the initial phases of said crystallized FcR protein.

81. A composition comprising FcγRIIa protein in a crystalline form.